What is claimed:

1. An isolated ADMP, cleaving the Glu^{373}-Ala^{374} peptide bond of an aggrecan core protein.

2. An isolated ADMP, wherein said ADMP has the property of cleaving the Glu^{373}-Ala^{374} peptide bond of the aggrecan core protein and wherein said ADMP consists of the following domains from the N-terminus to the C-terminus: 1) a propeptide domain containing a furin cleavage site, followed by 2) a metalloprotease domain, followed by 3) a disintegrin-like domain, and 4) a thrombospondin homologous domain.

3. A non-glycosylated ADMP according to claim 1 or 2 in isolated form.

4. An ADMP according to claim 1 or 2, having a molecular weight between about 35kD and about 120kD, as measured by SDS-PAGE.

5. An ADMP according to claim 1 or 2, having a molecular weight between about 45kD and about 100kD, as measured by SDS-PAGE.

6. An ADMP according to claim 1 or 2 having a molecular weight between about 50kD and about 98kD, as measured by SDS-PAGE.

7. An isolated nucleic acid selected from the group comprising:
   (a) a coding region of a gene encoding a native mammalian ADMP of claim 1;
   (b) a nucleic acid that is at least 80% identical to the nucleic acid of (a) and that encodes an ADMP;
   or

(c) a nucleic acid which is degenerate as a result of the genetic code to nucleic acid defined in (a) or (b) and which encodes an ADMP.

8. An isolated nucleic acid according to claim 7, wherein the ADMP is a human ADMP.

9. An isolated nucleic acid of claim 7 or 8 which encodes an active ADMP variant or ADMP derivative.

10. An ADMP according to claim 1 or 2, that has a molecular weight of about 98kD for the zymogen as measured by the SDS-PAGE.

11. An ADMP according to claim 1 or 2, that has a molecular weight of about 67kD as measured by SDS-PAGE for the mature form of the protease lacking the propeptide domain.

12. An isolated nucleic acid selected from the group comprising:

(a) a coding region of a gene encoding native mammalian ADMP of claim 10;

(b) a cDNA comprising nucleotides 406-2919 of SEQ ID NO:1;

(c) a nucleic acid that is at least 80% identical to the nucleic acid of (a) or (b) and that encodes an ADMP; or

(d) a nucleic acid which is degenerate as a result of the genetic code to nucleic acid defined in (a), (b) or (c) and which encodes an ADMP.

13. An isolated nucleic acid according to claim 12, wherein the ADMP is a human ADMP.

14. An ADMP according to claim 1 or 2 that has a molecular weight of about 93kD for the zymogen as measured by SDS-PAGE.

15. An ADMP according to claim 1 or 2, that has a molecular weight of about 50kD, 54kDa, 62kDa or 64kD as measured by SDS-PAGE for the mature protease lacking the propeptide domain.

16. A composition comprising an ADMP as in any of claims 1 or 2.

17. An isolated nucleic acid selected from the group comprising:
    (a) a coding region of a gene encoding native mammalian ADMP having a molecular weight of about 93kD as measured by SDS-PAGE;
    (b) a cDNA comprising nucleotides 121-2910 of SEQ ID NO:14;
    (c) a nucleic acid that is at least 80% identical to the nucleic acid of (a) or (b) and that encodes an ADMP and
    (d) a nucleic acid which is degenerate as a result of the genetic code to nucleic acid defined in (a),(b) or (c) and which encodes an ADMP.

18. An isolated nucleic acid according to claim 17, wherein the ADMP is a human ADMP.

19. An antibody that binds to an ADMP according to claim 1.

20. An antibody according to claim 19, wherein the antibody is a monoclonal antibody.

21. An expression vector that directs the expression of a nucleic acid sequence as in any of claims 7,8,12,13,17 or 18.

22. A host cell transfected or transformed with an

expression vector that directs the expression of a nucleic acid sequence as in any of claims 7,8,12,13,17 or 18.

23. A method for producing an ADMP, comprising:
(a) culturing a host cell under conditions promoting expression; and
b) recovering the ADMP from the culture medium.

24. ADMPs produced according to claim 23.

25. ADMP-1 comprising the sequence of amino acids 1-837 of SEQ.ID NO:2.

26. ADMP-2 comprising the sequence of amino acids 1-930 of SEQ.ID NO:15.

27. A method of identifying cell lines, cells or tissues that produce ADMPs using a nucleic acid probe which hybridizes with a native ADMP nucleic acid sequence according to any of claims 7,8,12,13,17 or 18 to detect ADMP message in biological samples.

28. The use of an ADMP according to any of claims 1 or 2 or 25 or 26 for three-dimensional structural analysis and computer-aided drug design of ADMP inhibitors.

29. A method of inhibiting the cleavage of aggrecan in a mammal comprising administering to such mammal an effective amount of a compound that inhibits the proteolytic activity of an ADMP as in any of claims 1 or 2 or 25 or 26.

30. A method for treating a mammal having a disease characterized by an overproduction or an up-regulated production of an ADMP comprising administering to the mammal a pharmaceutical

composition comprising an amount of a compound that effectively inhibits the proteolytic activity of an ADMP as in any of claims 1 or 2 or 25 or 26.

31. A method of inhibiting the cleavage of aggrecan in a mammal comprising administering to such mammal an effective amount of a compound that inhibits the isolated ADMP comprising the sequence of amino acids 1-837 of SEQ ID NO:2.

32. A method for treating a mammal having a disease characterized by an overproduction or an up-regulated production of an ADMP, comprising administering to the mammal a composition comprising an amount of a compound that effectively inhibits the ADMP activity of an enzyme comprising the sequence of amino acids 1-837 of SEQ ID NO:2.

33. A method of inhibiting the cleavage of aggrecan in a mammal comprising administering to such mammal an effective amount of a compound that inhibits the isolated ADMP comprising the sequence of amino acids 1-930 of SEQ ID NO:15.

34. A method of inhibiting the cleavage of aggrecan in a mammal comprising administering to such mammal an effective amount of a compound that inhibits the ADMP activity of an enzyme wherein the protein used is ADAMTS-1.

35. A method for treating a mammal having a disease characterized by an overproduction or an upregulated production of an ADMP, comprising administering to the mammal a composition comprising an amount of a compound that effectively inhibits the ADMP activity of an enzyme comprising the sequence of amino acids 1-930 of SEQ ID NO:15.

36. A method for treating a mammal having a disease characterized by an overproduction or an up-regulated production of an ADMP, comprising administering to the mammal a composition comprising an amount of a compound that effectively inhibits the ADMP activity of an enzyme wherein the protein used is ADAMTS-1.

37. An assay for ADMP activity and inhibitors of ADMPs, which comprises:

(a) generating soluble ADMPs, by stimulation of human or animal tissue or cells;

(b) detecting ADMP enzymatic activity by using the soluble ADMPs generated in (a) or any ADMP-containing sample, incubating with an aggrecan substrate in absence or presence of an inhibitor, and monitoring production of aggrecan fragments produced by specific cleavage at an ADMP-susceptible site using a neoepitope antibody to the new N-terminus or C-terminus generated by ADMP-mediated cleavage;

(c) evaluating inhibition of ADMP activity by comparing the amount of product produced in the presence versus absence of compound.

38. An assay according to claim 37 wherein the tissue or cell source of ADMPs is cartilage or chondrocytes.

39. An assay according to claim 37 or 38 wherein the aggrecan substrate is aggrecan isolated from human or animal tissue.

40. An assay according to claim 37 wherein the

aggrecan substrate is a recombinant aggrecan molecule or recombinant portion of the aggrecan molecule containing an aggrecanase-sensitive cleavage site.

41. An assay according to claim 40 wherein the recombinant portion of the aggrecan molecule contains the $E^{373-374}A$ bond.

42. An assay according to claim 40 wherein the recombinant aggrecan fragment contains the $E^{1545-1546}G$ bond.

43. An assay according to claim 40 wherein the portion of the aggrecan molecule contains the $E^{1714-1715}G$ bond.

44. An assay according to claim 40 wherein the recombinant portion of the aggrecan molecule contains the $E^{1819-1820}A$ bond.

45. An assay according to claim 40 wherein the recombinant portion of the aggrecan molecule contains the $E^{1919-1920}L$ bond.

46. An assay according to claims 37, 38, 40-45 wherein fragments produced by specific cleavage at the the $E^{373-374}A$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

47. An assay according to claims 37, 38, 40-45 wherein fragments produced by specific cleavage at the the $E^{1545-1546}G$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

48. An assay according to claims 37, 38, 40-45 wherein fragments produced by specific cleavage at the the $E^{1714-1715}G$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

49. An assay according to claim 37, 38, 40-45 wherein fragments produced by specific cleavage at the the $E^{1819-1820}A$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

50. An assay according to claim 37, 38, 40-45 wherein fragments produced by specific cleavage at the the $E^{1919-1920}L$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

51. An assay according to claim 37, 38, 40-45 wherein the ARGSV N-terminus is detected using the monoclonal antibody, BC-3.

52. A method for assaying compounds for activity against an ADMP comprising:

providing an ADMP and an ADMP substrate;

contacting said ADMP with a candidate inhibitory compound in the presence of said ADMP; and

measuring the inhibition of the ADMP activity.

53. A method for assaying compounds for activity against an ADAMTS-1 comprising:

providing an ADAMTS-1 and an ADAMTS-1 substrate;

contacting said ADAMTS-1 with a candidate inhibitory compound in the presence of said ADAMTS-1; and

measuring the inhibition of the ADAMTS-1 activity.

54. A method for diagnosing arthritic diseases in a mammal using an antibody according to claim 19 or 20 to detect ADMPs in biological samples.

55. An method for detecting ADMP-generated products in biological samples which comprises detecting the new N-terminus or new C-terminus on fragments produced by specific cleavage at an ADMP-sensitive site using a neoepitope antibody to the N-terminus or C-terminus on the ADMP-generated fragment.

56. An assay according to claim 55 wherein fragments produced by specific cleavage at the the $E^{373}\text{-}^{374}A$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

57. An assay according to claim 55 wherein fragments produced by specific cleavage at the the $E^{1545}\text{-}^{1546}G$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

58. An assay according to claim 55 wherein fragments produced by specific cleavage at the $E^{1714}\text{-}^{1715}G$ bond are monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

59. An assay according to claim 55 wherein fragments produced by specific cleavage at the $E^{1819}\text{-}^{1820}A$ bond are monitored using a neoepitope antibody to the new

C-terminus or new N-terminus on fragments generated by cleavage at this bond.

60. An assay according to claim 55 wherein produced by specific cleavage at the $E^{1919-1920}L$ bond is monitored using a neoepitope antibody to the new C-terminus or new N-terminus on fragments generated by cleavage at this bond.

61. A method for diagnosing arthritic diseases in a mammal by monitoring specific ADMP-generated aggrecan fragments in biological samples according to any of claims 55-60.

62 ~~61~~. A method for diagnosing arthritic diseases in a mammal using a nucleic acid probe which hybridizes with a native ADMP nucleic acid sequence according to any of claims 7,8,12,13,17 or 18 to detect ADMP message in biological samples.

63 ~~62~~. A method for diagnosing a disease in a mammal characterized by an overproduction or an up-regulated production of an ADMP using an antibody to detect ADMPs in biological samples.

64 ~~63~~. A method for diagnosing a disease in a mammal characterized by an overproduction or an up-regulated production of an ADMP by monitoring specific ADMP-generated fragments in biological samples according to any of claims 55-60.

65 ~~64~~. A method for diagnosing a disease in a mammal characterized by an overproduction or an up-regulated production of an ADMP using a nucleic acid probe which hybridizes with a native ADMP nucleic acid sequence according to any of claims 7,8,12,13,17 or 18 to detect ADMP message in biological samples.

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